## REMARKS

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

### I. Status of Claims

Claims 39, 40, 42-50 and 52-66 are pending in this application. Claim 50 is currently amended. No new claims have been added.

Applicants note that a listing of pending claims on form PTOL-326 omits claim 60 from the listing. However, page 3 of the Office Action indicates that claim 60 is rejected. Applicants respectfully submit that claim 60 is currently pending in this application.

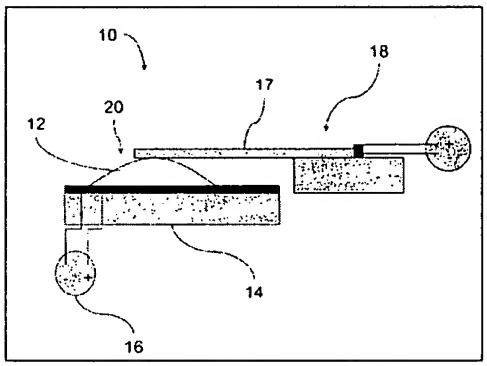
### II. Prior Art Rejections Should Be Withdrawn

Claims 39, 42-50, 52-66 are rejected under § 103(a) as being obvious over Porter (U.S. Patent 6,823,717) in view of Lee (U.S. Patent 5,872,372). Claims 40 and 60 are rejected under § 103(a) as being obvious over Porter in view of Lee and further in view of Tortonese. These rejections are respectfully traversed.

#### A. No teaching or suggestion to detect binding to the cantilever

Claims 39 and 50 both recite "a biofunctionalized cantilever" and "binding of a biological analyte to the cantilever." Neither Porter nor Lee teach or suggest binding of a biological analyte to a biofunctionalized cantilever. In fact, page 2 of the Office Action admits that "Porter et al., does not show a biofunctional cantilever." (emphasis added). Thus, Porter and Lee cannot render obvious claims 39 and 50 because "[t]o establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art." MPEP 2143.03 (citing *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974)) (emphasis added). Therefore, the rejections should be withdrawn.

In addition to failing to teach or suggest a biofunctionalized cantilever, Porter does not disclose binding of a biological analyte to a cantilever. For the Office's convenience, Figure 1 of Porter is reproduced below.




Porter discloses binding of a biological analyte to a substrate (14) via a sensing material (12). (column 6, lines 18-25 and column 11, lines 39-44). As clearly shown in Figure 1 of Porter, the substrate (14) is a distinct and separate component apart from the deflectable arm (17) of a microcantilever (18). Therefore, Porter does not teach or suggest "binding of a biological analyte to the cantilever," as recited in claims 39 and 50 of the claimed invention. Even though the sensing material (12) appears to be in physical contact with the deflectable arm (17) in Figure 1 of Porter, mere touching of the sensing material to the deflectable arm does not constitute "binding of a biological analyte to the cantilever."

Nowhere does Porter teach or suggest omitting the substrate (14) from the sensor (10) while providing analyte binding to a biofunctionalized deflectable arm (17). In fact, Porter's repeated mentioning that the sensing material (12) must undergo a volumetric expansion in the vertical direction (col. 11, lines 41-42; col. 13, line 52; col. 14, lines 1-3; col. 14, lines 19-20; col. 14, line 27) indicates that the Office's proposed modification of Porter's device would impermissibly "change the principle of operation of the prior art invention being modified." M.P.E.P. § 2143.01. Porter's device would not work without the underlying substrate (14) because it provides a stationary point of reference for the sensing material's volumetric expansion in the vertical direction up towards the deflectable arm (17) positioned above the substrate (14). The proffered modification is therefore improper.

Page 2 of the Office Action states that it would have been obvious to "modify" the device in Porter to achieve the claimed invention and refers to column 18, lines 25-34 of Porter as an example of the reference's ability to be modified. But, the "mere fact that references can be . . . modified does not render the resultant combination obvious unless the prior art also

suggests the desirability of the combination." M.P.E.P. § 2143.01 (citing *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990)).

In fact, using a scanning force microscope (SFM) to help "save[] the cantilever from damage" is completely unnecessary in the claimed invention. Porter uses the SFM because the sensing material is located on the underlying substrate rather than on the cantilever itself. The SFM is used to carefully position two separate components, i.e., the underlying substrate and the cantilever arm. By contrast, the claimed invention circumvents this problem of precise relative positioning of two components by allowing the underlying substrate to be omitted altogether. In claims 39 and 50 of the present application, the binding occurs to the "biofunctionalized cantilever" rather than to the underlying substrate. The claimed invention omits Porter's substrate while retaining the ability to provide a biofunctionalized layer to which an analyte may bind. This is an indicia of unobviousness. M.P.E.P. § 2144.04 (stating that "the omission of an element and retention of its function is an indicia of unobviousness") (citing *In re Edge*, 359 F.2d 896, 149 USPQ 556 (CCPA 1966)) (emphasis in original). Therefore, Porter's use of SFM does not teach or suggest omitting the substrate and biofunctionalizing the cantilever.

Applicants respectfully request a withdrawal of the rejections over Porter. Tortonese was applied only against dependent claims 40 and 60. Thus, Tortonese does not remedy the deficiencies of Porter.

**B. No motivation to combine Lee's transistor with Porter's sensor**

A person skilled in the art would not have combined the transistor of Lee with the sensor of Porter to achieve the claimed invention. The Office Action asserts that metal piezoresistors on a substrate are notoriously known. However, the use of a metal film as a strain gauge in a cantilever type biosensor is not disclosed in the applied prior art references and is thus not notoriously known from the prior art used in the rejection.

First, there is no motivation in either Lee or Porter to use the piezoresistive channel in Lee's transistor as the strain gauge in Porter's biochemical sensor. Column 11, line 58 of

Porter teaches a barium titanate piezoresistor deflection detector or strain gauge for measuring a deflection of the cantilever. Barium titanate is a ceramic oxide having the formula $BaTiO_3$. Lee does not teach or suggest to substitute a ceramic piezoresistor deflection detector on a cantilever type biodetector or chemical detector with a piezoresistive transistor or with a metal film. The transistor of Lee is a switching device. It is not used to detect a deflection of a cantilever. Thus, one of ordinary skill in the art would not be motivated to use the transistor of Lee in the device of Porter because Lee does not teach to use the transistor to detect a deflection of a cantilever.

Second, combining the transistor in Lee with the sensor in Porter would "change the principle of operation of the prior art invention being modified." M.P.E.P. § 2143.01. Lee's piezoresistive transistor channel layer operates on the principle of detecting a force applied to itself, whereas Porter's barium titanate piezoresistor measures the deflection of the cantilever. By using the channel material in Lee as the strain gauge in Porter's sensor, one would impermissibly "change the principle of operation" of Lee's channel layer, namely the detection of a force applied only to the channel layer.

While the Office Action asserts that metallic piezoresistors are notoriously known, their combination with microcantilevers is not. While microcantilevers with piezoresistive detection have been known since at least 1991 (see Tortonese paper ref 12), but in the 16 years since, there has been almost no mention of the combination of metallic piezoresistors with microcantilevers in the prior art and applicants are not aware of prior art commercial devices using this combination. There are a number of reasons why those of ordinary skill in the art would generally not find using metal piezoresistors for biofunctionalized cantilevers obvious.

First, those skilled in the art are always seeking the most sensitive detection with microcantilevers. Metal films have a much lower gauge factors than semiconductor piezoresistors and hence are considered less sensitive by those in the art.

Second, since microcantilevers are often made out of silicon, this makes adding a semiconductor piezoresistor natural by simply doping a portion of the microcantilever. Thus, a separate metal deposition and patterning step is not needed. In the 2nd paragraph of the Tortonese paper, the authors state that "Silicon exhibits a strong piezoresistive effect. At the same time it is a suitable material for fabricating cantilever beams."

Third, some of the attendant advantages that come with using metallic piezoresistors that are disclosed in the present application are not obvious to those skilled in the art because they are specific to microdevices and, in fact, microcantilevers that are even smaller than those being produced commercially today.

For example, one of the advantages is being able to make low impedance (e.g. 50 ohm) devices for high frequency applications. While it is easy to make a low impedance semiconductor strain gauge at large scales, as the device dimensions reach micron scales and below, the resistance of semiconductor piezoresistors gets very large. Furthermore, semiconductor strain gauges also exhibit much worse low frequency noise as the dimensions of the doped region become small. As cantilever thicknesses go to a few tens of nanometers, the volume of the piezoresistor will be so small that the small number of electrical carriers in the semiconductor will cause lots of low frequency noise. The present inventors realized that using metals instead of semiconudctors reduce or eliminate this noise in small scale devices. The present inventors realized that only a simple metal film is required to reduce or eliminate noise and this makes device fabrication easier and manufacturing costs low. This is not taught or appreciated by the applied prior art.

Therefore, Applicants respectfully request a withdrawal of the rejections in view of Porter and Lee.

**C. No teaching or suggestion of metal films of claims 47 and 57**

Claims 47 and 57 recite "a pure metal composition selected from the group consisting of Au, Cr, Ag, Pd, Ni, Pt, or Mn, or alloys selected from the group consisting of Au-Ni, NiCr,

Bi-Sb, Ag-Ni, Cu-Ni, or Pt-Cr." Page 3 of the Office Action refers to Lee for motivation to use a thin metallic piezoresistor.

However, Lee only discloses thin films made of a Mo–C compound (i.e., a metal carbide). Thus, neither Lee nor Porter teach or suggest the actual compounds recited in claims 47 and 57.

## III. Conclusion

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested. The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

Respectfully submitted,

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The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. § 1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.